II. REMARKS

Preliminary Remarks

Reconsideration and allowance of the present application based on the following remarks are respectfully requested. The examiner has renumbered claims 23-40 as claims 22-39. Accordingly, claims 22-39 are currently pending in this application. Claims 22, 27, 29, 34, 38, and 39 have been allowed. Claims 23 and 30 are objected to while claims 24-26, 28, 31-33 and 35-37 remain at issue.

Claim 23 was objected to by the examiner under 37 C.F.R. §1.75 for being a substantial duplicate of claim 22. The applicants have cancelled claim 23 without prejudice as the same subject matter is allowed in claim 22.

Claim 30 was objected to by the examiner under 37 C.F.R. §1.75 for being a substantial duplicate of claim 29. The applicants have cancelled claim 30 without prejudice as the same subject matter is allowed in claim 29.

The examiner objected to claims 24-26 and 31-33 under 37 C.F.R. §1.75(c) as being improperly dependent claims. Accordingly, the applicants have amended claims 25, 26, 31 and 32 in proper dependent forms to either claims 22 or 29.

Amended claims 25 and 26 are now directed to the isolated polynucleotide of claim 22 wherein said amino acid sequence is at least 90% or 95% identical to that of SEQ ID NO: 2 and having the same enzymatic activity as a component H polypeptide of the phosphotransferase system. Support for "having the same activity has a component H polypeptide of the phosphotransferase system" can be found on page 4, lines 5-19, and page 5, lines 4-11.

Amended claims 32 and 33 are now directed to the isolated polynucleotide of claim 29 wherein said amino acid sequence is at least 90% or 95% identical to that of SEQ ID NO: 4 and having the same enzymatic activity as a component H polypeptide of the phosphotransferase system. Support for "having the same activity has a component H polypeptide of the phosphotransferase system" can be found on page 5, lines 4-11 and page 11, lines 11-16.

The applicants do not intend by these or any amendments to abandon subject matter of the claims as originally filed or later presented, and reserve the right to pursue such subject matter in continuing applications.

Patentability Remarks

Rejection Pursuant to 35 U.S.C. §112, First Paragraph, Written Description

In paragraph 7 of the official action, the examiner has rejected claims 25, 26, 28, 31-33, and 35-37 under 35 U.S.C. § 112, first paragraph, for lacking written description. Specifically, the examiner alleged that the specification only provides an isolated polynucleotide consisting of SEQ ID NO: 1 or SEQ ID NO: 3, and a polypeptide consisting of SEQ ID NO: 4 with no disclosure to any particular structure to function/activity relationship in the single disclosed species. Furthermore, the examiner asserted that the specification fails to describe additional representative species of these polynucleotides by any identifying structural characteristics or properties. The examiner concludes that the applicants have failed to sufficiently describe the representative species encompassed by claims 25, 26, 28, 31-33, and 35-37.

Solely for the purpose of expediting prosecution, and without prejudice to the applicants' right to seen broader claims in a continuing application, the applicants have canceled claims 28, 31, and 35 without prejudice, thereby obviating the rejection of these claims.

New independent claims 25, 26, 32, and 33 are directed to isolated polynucleotides that are at least 90% or 95% identical to a polynucleotide encoding the amino acid sequence of SEQ ID NOs: 2 or 4 and having the same enzymatic activity as a component H polypeptide of the phosphotransferase system. These structural and functional characteristics of the subject matter of amended claims 25, 26, 32, and 33 meet the Written Description Guidelines of the United States Patent Office (February, 2000). In particular, Example 14 of the guidelines states that a claimed variant polynucleotide that has a high percent identity to a sequence taught in the specification, along with a functional limitation that the claimed variant polynucleotides encode variant polypeptides that exhibit a specified catalytic activity, meet the written description if the required activity can be determined as described in the specification. In the instance claims, the claimed variants must each be at least 90% or 95% identical to SEQ ID NO: 2 or 4 (see page 5, lines 4-11 and page 11, lines 11-16) and encode a polypeptide that has the same enzymatic activity as a component H polypeptide of the phosphotransferase system. The biological activity of the component H polypeptide of the

phosphotransferase system as well as the protein phosphorylation assays to measure component H phosphorylase enzymatic activity were well known in the art at the time of filing applicants' invention (See Exhibit 1 Galinier *et al., Proc. Natl. Acad. Sci. USA*, 94:8439-8444 (1997) and Herzberg, O. and R. Klevit, *Cur. Opin. in Struc. Biol.*, 4:814-822 (1994), Deutscher *et al., FEMS Microbiol. Lett.* 23:157-162 (1984) and Reizer *et al., J. Bacteriol.* 160:333-340 (1984)).

Furthermore, the specification teaches variants of SEQ ID NO: 2 wherein the L-alanine in position 25 of SEQ ID NO: 2 was replaced by an L-threonine and this replacement enhanced the enzymatic activity of the component H of the phosphotransferase system (See page 11, lines 11-16). The applicants further outline conventional mutagenesis methods to generate further mutants as long as component H of the phosphotransferase system maintains its enzymatic activity (see page 5, lines 4-16; page 11, line 23 to page 12, line 17).

In addition, the specification teaches that upon enhancement of expression of the *pts*H gene, coryneform bacteria also enhance their production of amino acids like lysine. Example 5 demonstrates this correlation. Specifically, *pts*H gene vector expression allowed *C. glutamicum* strain DSM5715::pEC-K18mob2ptsHexp to increase its lysine production (see Table 1).

Accordingly, the structural and functional limitations of claims 25, 26, 31, and 32 are described in the specification in such a way as to convey to one of skill in the art that the applicants had possession of a finite number of claimed polynucleotides and the means to measure such activity.

Claims 35-37 ultimately depend from claims 25, 26, 31, and 32 (*e.g.*, vectors comprising such a polynucleotide, host cells comprising such vectors, and deposit strains) and therefore are fully described in the specification.

In view of the foregoing amendments and remarks, the applicants submit that the rejection of claims 25, 26, 28, 31-33, and 35-37 pursuant to 35 U.S.C. § 112, first paragraph, for lack of written description, has been overcome and should be withdrawn.

Rejection Pursuant to 35 U.S.C. §112, First Paragraph, Enablement

In paragraph 8 of the official action, the examiner rejected claims 24-26, 28, 31-33, and 35-37 under 35 U.S.C. §112, first paragraph, for lacking enablement. Specifically, the examiner stated that while the isolated polynucleotide encoding a polypeptide comprising the amino acid sequence of SEQ ID NO: 2 or an isolated polynucleotide comprising SEQ ID NO:

1 is enabled by the specification, the specification does not teach the specific structural/catalytic amino acids and the structural motifs essential for protein activity/function which must be preserved. The examiner further asserted the specification does not teach an assay to determine whether a variant polypeptide has enzymatic activity and therefore, one of skill in the art could only make the invention with undue experimentation. In view of the foregoing amendments, the applicants respectfully traverse the enablement rejection.

Solely for the purpose of expediting prosecution, and without prejudice to the applicants' right to seek broader claims in a continuing application, the applicants have canceled claims 24, 31, and 35 thereby rendering moot the rejection as applied to each of these claims.

The issue of enablement involves the question of whether an application enables one of ordinary skill in the art to make and to use the claimed invention. Experimentation is limited in claims 25, 26, 32, and 33 to nucleic acids encoding polypeptides containing an amino acid sequence which is at least 90% (or 95% identical in claims 26 and 33) identical to the amino acid sequence of SEQ ID NO: 2 (claims 25 and 26) or SEQ ID NO: 4 (claims 32 and 33), and exhibit the same enzymatic activity as a component H polypeptide of the phosphotransferase system. Therefore, there is no question that the variants encompassed by the claims must retain the utility of the DNA sequence discovered and claimed by the applicants. The applicants further submit the specification enables one of skill in the art to make and functionally define the claimed variants.

Specifically, claims 25, 26, 32, and 33 satisfy the "how to make" prong of the enablement requirement because the scope of the claim is "reasonable correlated" with the teachings in the application [See MPEP §2164.01b]. The application and ordinary skill permit one skill in the art to make any polynucleotide having 90% or greater sequence identity to the sequence recited in the claims using PCR technology or other mutagenesis techniques as discussed on page 8, lines 17-32, and page 11, line 11 to page 12, line 21. In fact, the Patent Office's own written description training materials acknowledge that "procedure[s] for making variants of [a protein having] SEQ ID NO: 3 which have 95% identity to SEQ ID NO: 3 and retain its enzymatic activity are conventional in the art." (See Revised Interim Written Description Guidelines Training Materials, Example 14). Moreover, the application provides guidance as to the types of changes (*e.g.*, conservative mutations) that are more likely to retain functionality (see specification, page 11, lines 11-22, and page 7, line 31 to page 8, line 14).

With regard to the examiner's comments that the structural and catalytic motifs for the component H (or HPr) protein were not taught by the specification or known at the time of filing, the applicants assert that both the catalytic and structural characteristics of the component H (or HPr) protein were well known in the art well before the filing date of applicants' invention (See Exhibit 2, Herzberg *et al., Current Opinion in Structural Biology*, 4:814-822 (1994)). Both NMR and crystal structures for the component H protein (HPr) have been studied in both Gram positive and Gram negative bacteria (*See* Herzberg *et al.*, at page 816, first column). The amino acid sequence encoding the component H protein shares a strong sequence identity across both Gram negative and Gram positive bacteria. In addition, these sequences encoding the component H protein have virtually the same catalytic and overall crystal structure properties (*See* Herzberg *et al.* at page 815 and 816). For example, the active site of the component H protein (or HPr) has a consensus amino acid sequence at position 12-18 of X12-Gly13-Leu/Ile14-His15-Ala/Thr16-Arg17-Pro18, where X is any amino acid. **Both SEQ ID NOS: 2 and 4 share this same consensus active site sequence**. A change in any of these amino acids, especially His 15 and Arg 17, would inactivate the phosphorylation activity of HPr (*See* Herzberg *et al.* at page 816, second column).

In addition, the variants recited in claims 25, 26, 32 and 33 are also functionally defined in that the claimed variants are limited to those with the same enzymatic activity as a component H polypeptide of the phosphotransferase system (HPr activity) (i.e., accepting phosphates from E1 like protein, and donating phosphate to EIIA like proteins). The specification specifically refers to the inventors successfully isolating the novel ptsH gene coding for the component H enzyme from C. glutamicum (page 7, lines 24-30, and Example 2). The specification also specifically describes the variant polypeptides with at least 90-95% identity to the polypeptide according to SEQ ID NO: 2 and SEQ ID NO: 4 must have component H enzymatic activity (page 5, lines 4-11, and page 11, line 30 to page 12, line 8). Accordingly, the structural and catalytic properties of HPr were well known to those skilled in the art at the time of filing and thus, the specification's requirement that the variants maintain component H enzymatic activity is fully enabled by the specification.

Component H or HPr activity can be assessed by a routine screening assay known in the art at the time of filing that identifies those encoded polypeptides with the enzymatic activity (component H phosphatase enzymatic activity) as recited in the claims (Exhibit 1, Deutscher *et al., FEMS Microbiol. Lett.* 23:157-162 (1984) and Reizer *et al., J. Bacteriol.* 160:333-340 (1984)). Since the component H assay is routine in the art, one of skill could

perform this assay without undue experimentation. For example, the component H assay is performed first by isolating HPr kinase isolated from extracts of *C.glutamicum* cells using a DEAE-5PW Protein PAK glass column equilibrated with TrisHCl and eluted with an increasing concentration of NaCl solution. The partially purified HPr kinase is incubated with applicants novel protein HPr and radiolabeled ATP [γ-^{32}P] and the HPr products are run on a SDS PAGE gel. Only active phosphorylated HPr, labeled with P^{32}, will be detected (See Exhibit 1, Galinier *et al., Proc. Natl Acad. Sci USA* 94:8439-8444 (1997)).

Finally, as discussed above, Example 5 is an indirect method which enables one of skill in the art to directly correlate the functionality of component H in a 90% or higher variant by measuring lysine production in comparison to a wild type strain with no enhanced component H enzymatic activity. Accordingly, in view of the structural and functional information about the claimed polynucleotides that is provided in the instant application, along with the teachings in the prior art regarding crystal structures of the component H protein as well as component H assays (HPr), the applicants submit that claims 25, 26, 32, and 33, their dependents (claims 36 and 37) are supported by an enabling disclosure.

In order to expedite prosecution and without prejudice to the applicants' right to seek broader claims in a continuing application, claims 24, 30, and 35 have been cancelled without prejudice thereby obviating the rejection of this claim. Claims 36 and 37 are ultimately dependent upon claims 25, 26, 32, and 33, and therefore are also fully enabled by the specification.

In light of the foregoing amendments and remarks, the applicants submit that the rejection of claims 24-26, 28, 31-33, and 35-37 under 35 U.S.C. §112, first paragraph, for lack of enablement, has been overcome and should be withdrawn.

Rejection Under 35 U.S.C. §112, Second Paragraph, Indefiniteness

The examiner rejected claims 31-33 under 35 U.S.C. §112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which the applicants regard as the invention. Specifically, the examiner alleged that claims 31-33 recite the limitations of 80%, 90%, and 95% identity to SEQ ID NO: 2 which lacks insufficient antecedent basis since claim 30 refers to SEQ ID NO: 4.

As stated above, the applicants have cancelled claim 31 without prejudice. Claims 32 and 33 are now directed to the isolated polynucleotide of claim 29 wherein said amino acid sequence is at least 90% or 95% identical to that of SEQ ID NO: 4 and having the same

enzymatic activity as a component H polypeptide. Accordingly, these claims have proper antecedent basis to claim 29 which is directed to an isolated polynucleotide comprising nucleotides encoding a protein with the amino acid sequence of SEQ ID NO:4. In view of the foregoing amendments and remarks, the applicants respectfully submit that the rejection of claims 31-33 under 35 U.S.C. §112, second paragraph, have now been overcome and should be withdrawn.